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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/360,242	07/22/1999	JOHN R. MCDONALD	25020-601B	3887

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EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	PAPER NUMBER
1647	39

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/360,242	MCDONALD ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29,31,32,34-38,40,42,44-46,48-54,57 and 65-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29,31,32,34-38,40,42,44-46,48-54,57 and 65-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. The Declaration under 37 CFR 1.132 by John McDonald, filed 10/25/02, has been entered into the record.

B. The Supplemental Information Disclosure Statement, filed 9/12/02, has been entered into the record. However, reference AH has been lined through since it does not provide a date of submission for the deposit.

C. Claims 26-29, 31, 32, 34-38, 40, 42, 44-46, 48-54, 57 and 65-87 are pending in the application. In Amendment E, filed 10/15/02, Applicants have added new claims 88-91. Therefore, claims 26-29, 31, 32, 34-38, 40, 42, 44-46, 48-54, 57 and 65-91 are pending in the application.

D. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 26-29, 31, 32, 34-38, 40, 42, 44-46, 48-54, 57, 65-87 remain rejected and new claims 88-91 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 2-3 of the Office Action dated 4/9/02. Applicants provide a Declaration and argue that this information provides a nexus between in vitro and in vivo data. Applicants also provide numerous references showing that a mouse xenograft model is a recognized model that is used to assess the in vivo efficacy of antitumor agents and that immunotoxins and cytotoxic conjugates have been widely shown to possess pharmacological activity. Applicants also argue on page 25 of the response that chemokine receptors are elevated in a variety of pathologies and are elevated in patterns characteristic of a particular disease and in a temporal manner in a disease and that the instant application provides sufficient evidence that chemokine-receptor targeting conjugates possess specificity for, and activity against, target chemokine-receptor-bearing cells. However, the data disclosed in this Declaration is not persuasive to demonstrate enablement of the present invention since enablement must be demonstrated in the specification *as originally filed*. There is no data in the original specification showing that any of the chemokine-toxin conjugates have any affect on activated immune effector cells in vivo. Applicants have only shown that some of these conjugates are active in an RIP assay (Example 2). Applicants do discuss using a mouse xenograft model in the original specification, but there is no data showing that the conjugates are effective

in this model. Therefore, the Declaration after the fact cannot be used to establish enablement of the present invention at the time of filing.

Furthermore, even if this Declaration was persuasive, Applicants would still not be enabled for treating all pathological conditions by treating the underlying pathology. Beginning on page 26 of the response filed 10/15/02, Applicants argue that a considerable amount of experimentation is permissible, particularly if it is routine. Applicants argue that the breadth is not excessive, that the skill in the art is high, that the specification discusses in great detail that the activation, migration and proliferation of leukocytes are the hallmark of a vast number of immunomodulatory diseases and that the specification provides sufficient guidance and working examples of receptors and agents involved with potential treatment of numerous diseases. Potential disease which Applicants claim are treatable with their claimed methods can be seen in claims 31 and 32. This list, respectfully, is a comprehensive 'laundry list' of immune diseases and there is no guidance in the specification as to how one would go about treating each of these diseases. Though these diseases may all involve leukocytes, the pathologies are not identical, since, obviously, they are all different diseases and would require different modes of intervention. Applicants provide a long list of toxins in the specification (Table 4 and pages 81-82) are claiming the use of a large list of chemokines (claim 68) and chemokine receptors (claims 70 and 71), but there is no guidance of which combinations of chetoxins and conjugates to use for which disease. The number of possible combinations of chemokines and toxins is immense. Applicants argue that selection of this chemokine pathway is not new and that the specification details a variety of diseases and identifies the appropriate receptors to target. Applicants argue that this information, coupled with the exemplification of a dozen different conjugates in the specification, provides more than adequate guidance to practice the claimed invention. These arguments have also been considered, but are not deemed persuasive. Applicants may have disclosed numerous conjugates in the specification, but they nave not shown that these conjugates are effective in vivo to treat the underlying pathology of any disease. The fact that conjugates and the mouse xenograft model were known at the time of the present invention does not enable the present invention. Applicants have only shown in the Declaration that two compounds are effective in a mouse xenograft model. Applicants, respectfully, are claiming a "magic bullet" to treat all diseases with an underlying pathology. However, according to a paper cited by the Applicants (Idrugs 4(4):427-442, 2001), in which the present inventor is an author, it is stated that "few generalizations about chemokines prove to be entirely valid..." (i.e. it is unpredictable; page 431, right column, last paragraph). They also state that "it is important to establish the biological and clinical profile of a given chemokine on a case-by-case basis. This is especially true if the ratio, absolute number, and activation status of the

chemokine's target cells change during the course of the injury or disease." Therefore, not only have Applicants not enabled the treatment (e.g. which conjugates to use) for the expansive number of diseases, but they have also not taught (only speculated) how to alter this treatment regimen, or when and which conjugates to use throughout the treatment period, given that the treatment (i.e. types of conjugates) would likely need to change.

Therefore, in summary, the breadth of the claims is excessive with regard to Applicants claiming a method of treating the underlying pathology. Furthermore, there is a lack of guidance and working examples in the specification as originally filed with regards to the use of these conjugates in treating any disease in vivo. These, along with the lack of predictability to the artisan which conjugates to use for what diseases and at what point in the treatment, leads the Examiner to maintain that undue experimentation would be necessary to practice the invention as claimed.

3. Claim Rejections - 35 USC § 102

A. All rejections under 35 USC 102 in view of Volk et al. have been withdrawn in view of Applicants' arguments and the Declaration which discuss the differences between cytokines and chemokines.

4. Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 26-29, 34-38, 40, 44-46, 48-54, 57, 65-91 are rejected under 35 U.S.C. 102(b) as anticipated by Roby et al. (Oncology Reports 3:175-179, 1996), or in the alternative under 35 USC 103(a) as obvious over Roby et al. The claims recite a method of treating a pathological condition

Claim(s) 26-29, 34-38, 40, 44-46, 48-54, 57, 65-91 recite a method for treating a pathological condition by administering a chemokine-toxin conjugate to an animal wherein the conjugate is internalized by a cell. Roby et al. teach a chemokine-cytokine conjugate (MGSA/GROα-daunorubicin) which can be used to treat melanoma (Introduction and last paragraph of Discussion). However, the claims require the limitation that the conjugate must be internalized into a cell. Roby et al. teach the limitations of a chemokine-toxin conjugate which can be used to treat melanoma, as claimed in the instant application but does not mention the characteristic or property that the conjugate is internalized in a cell as claimed. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. With these conditions, where the (product or apparatus or method or product by process) seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
January 14, 2003